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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,466	01/26/2004	Sachiko Machida	690115.401C1	8356

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EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/765,466	MACHIDA ET AL.	
	Examiner	Art Unit	
	MELANIE YU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,17,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,17,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 October 2008 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 17, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's amendment recites "the receptor protein is non-glycosylated". There is insufficient support for this limitation in the specification. It is noted that the specification, at paragraph 85 teaches that a protein may be glycosylated, but does not teach a non-glycosylated protein. Although examples 3 and 4 do not specifically teach the glycosylation of LOX-1 receptor proteins, the examples do not specifically state that the LOX-1 receptor proteins are non-

glycosylated. The amendment reciting a non-glycosylated receptor protein is new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holtzman (US 5,969,123) in view of Schatz (US 5,932,433) further in view of Tall et al. (US 6,756,228).

Holtzman teaches a biochip for a screening assay (col. 12, lines 7-8) comprising a biotinylated receptor protein immobilized via a factor capable of specifically binding to biotin (streptavidin specifically binds to biotin and the biotinylated proteins is immobilized to the streptavidin, col. 12, lines 8-16), wherein the receptor protein comprises a biotinylation sequence motif (biotinylated protein comprises biotinylation sequence motif, col. 12, lines 11-16), and wherein the receptor protein has the ability of

being specifically bound by a ligand of the receptor protein (col. 8, line 65-col. 9, line 6). Holtzman fails to teach the biotinylation of the receptor protein carried out within a bacterial host and the receptor specifically being LOX-1.

Schatz teaches a recombinantly expressed biotinylated receptor protein immobilized via a factor capable of specifically binding to biotin (peptides are biotinylated and bound to streptavidin which specifically binds to biotin, col. 8, lines 10-27, biotinylated peptide may be a protein, col. 6, lines 13-19), wherein the receptor protein comprises a biotinylation sequence motif (when peptides are biotinylated, they gain a biotinylation sequence motif, col. 8, lines 10-27; col. 4, lines 57-60), wherein the biotinylation of the receptor protein has been carried out within a bacterial host instead of in vitro (carried out in *E. coli* host cells, col. 3, lines 47-50; col. 8, lines 10-14), in order to provide a protein that has been biotinylated.

Tall et al. teach a LOX-1 receptor immobilized to a substrate (col. 12, lines 29-38; col. 11, line 52-col. 12, line 57) wherein the LOX-1 receptor binds to an endogenous ligand (oxidized-LDL, col. 11, lines 39-51), in order to detect the presence of LOX-1 activity. Although Tall et al. do not specifically teach the LOX-1 receptor being non-glycosylated, Tall et al. do not disclose any type of alteration or glycosylation of the LOX-1 receptor and is therefore non-glycosylated.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the biotinylation of the receptor protein of Holtzman, biotinylation in vivo instead of in vitro as taught by Schatz, in order to provide a simplified biotinylation process (Schatz, col. 2, lines 59-63). It would have further

been obvious to one having ordinary skill in the art at the time the invention was made to include as the receptor protein of Holtzman in view of Schatz, a receptor protein of LOX-1 as taught by Tall et al., because Holtzman is generic with respect to the immobilized receptors that can be incorporated into the chip and one having ordinary skill in the art would be motivated to use the appropriate receptor ligand for detection of a desired analyte and to indicate increased or decreased susceptibility to atherosclerosis. Although Holtzman in view of Schatz further in view of Tall et al. fail to specifically teach the immobilized receptor protein obtained by refolding a biotinylated receptor protein expressed as an inclusion body within the host, such a limitation is drawn to a method of making the protein on the chip. The instant claims encompass a product of the receptor chip and not a method of making the product, the LOX-1 immobilized on the chip as taught by the prior art must be the same receptor protein required by the claims. Since the combination of prior art references described above, teaches a LOX-1 receptor protein biotinylated in a bacterial host and then immobilized on the substrate via the biotinylation sequence motif, the combination of the prior art references teaches the required structural limitations of the claim and the LOX-1 protein of the prior art reads on the claimed LOX-1 protein.

2. Claims 17 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brigham-Burke et al. (US 5,395,587) in view of Holtzman (US 5,969,123) further in view of Schatz (US 5,932,433) and Tall et al. (US 6,756,228).

Brigham-Burke et al. teach a protein immobilized on a SPR substrate (sensor chip, col. 5, lines 29-35; col. 5, lines 10-23) that conforms to a shape of an insertion site

of a surface plasmon resonance device (sensor chip fits through a slot in the housing for SPR detection, 14, Fig. 1; col. 5, lines 30-35), but fail to teach the protein being biotinylated and immobilized via a factor capable of binding specifically to biotin.

Holtzman in view of Schatz further in view of Tall et al., as applied to claim 1, teach a biotinylated receptor protein immobilized on a substrate via a factor capable of specifically binding to biotin, in order to provide immobilization of receptor proteins on a substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include on the substrate of Brigham-Burke et al., an immobilization technique of a biotinylated receptor protein as taught by Holtzman in view of Schatz further in view of Tall et al., in order to simple and efficient immobilization of proteins on a substrate.

3. Claims 17 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muramatsu (Piezoelectric Crystal Biosensor Modified with Protein A for Determination of Immunoglobulins, 1987, Analytical Chemistry, vol. 59, pages 2760-2763) in view of Holtzman (US 5,969,123) further in view of Schatz (US 5,932,433) and Tall et al. (US 6,756,228).

Muramatsu teaches a protein immobilized on a crystal oscillator (pg. 2760, right column, last paragraph), but fail to teach the protein being biotinylated and immobilized via a factor capable of binding specifically to biotin.

Holtzman in view of Schatz further in view of Tall et al., as applied to claim 1, teach a biotinylated receptor protein immobilized on a substrate via a factor capable of

specifically binding to biotin, in order to provide immobilization of receptor proteins on a substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include on the substrate of Muramatsu, biotinylation of a protein receptor and immobilization via a factor capable of binding specifically to biotin as taught by Holtzman in view of Schatz further in view of Tall et al., in order to simple and efficient immobilization of proteins on a substrate.

Response to Arguments

3. Applicant's arguments filed 14 October 2008 have been fully considered but they are not persuasive.

4. Applicant argues that the amendment to claim 1 requiring a non-glycosylated LOX-1 receptor protein is not new matter because the specification teaches that glycosylation "can be performed". Applicant's argument is not persuasive because while the instant specification teaches that the protein can be glycosylated, nowhere does the instant specification teach a non-glycosylated LOX-1 receptor protein.

5. Applicant argues that the cited references fail to teach a receptor chip comprising an immobilized scavenger receptor LOX-1, wherein the receptor protein is non-glycosylated. Applicant's argument is not persuasive because applicant does not specifically point out where Tall et al. teach that the LOX-1 receptor is glycosylated. Since Tall et al. do not teach that the LOX-1 receptor proteins are glycosylated and according to applicant's arguments at page 5, the naturally occurring state of a LOX-1

receptor protein is non-glycosylated, the LOX-1 receptor of Tall et al. is non-glycosylated.

6. Applicant further argues that the present applicant provides data indicated the unexpected results that non-glycosylated LOX-1 of the present invention binds to both AcLDL and OxLDL with a high affinity. Applicant's argument is not persuasive since the LOX-1 receptor of Tall et al. is also non-glycosylated the protein would also have the same high binding affinity. Furthermore, the instant specification does not attribute the high binding affinity to the non-glycosylation of the LOX-1 protein.

7. Applicant also argues that it would not have been obvious to one having ordinary skill in the art at the time the invention was made to use non-glycosylated LOX-1 to bind to its ligand because it was known in the art that non-glycosylated LOX-1 has substantially reduced binding affinity for its endogenous ligand as taught by Kataoka et al. (Journ. Biol. Chem., 2000;275(9):6573-6579). Applicant's argument is not persuasive because Kataoka et al. focus on a SR-PSOX receptor for binding OxLDL and at page 40666, left column, second sentence, specifically teach that LOX-1 is an entirely different receptor for OxLDL than SR-PSOX. Applicant's argument is also not persuasive because Tall et al. teach that LOX-1, in non-glycosylated form as discussed above, is an acceptable receptor for binding OxLDL. Therefore one having ordinary skill in the art would have recognized from this teaching that non-glycosylated LOX-1 has an acceptable affinity for binding OxLDL.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELANIE YU whose telephone number is (571)272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melanie Yu/
Patent Examiner, Art Unit 1641